Join A Breakthrough Canine Clinical Trial

SYNCHRONISATION OF IMMUNOTHERAPY

USING SERIAL C-REACTIVE PROTEIN (CRP) MEASUREMENTS IN DOGS

BIOTEMPUS

OWNERS INFORMATION GUIDE

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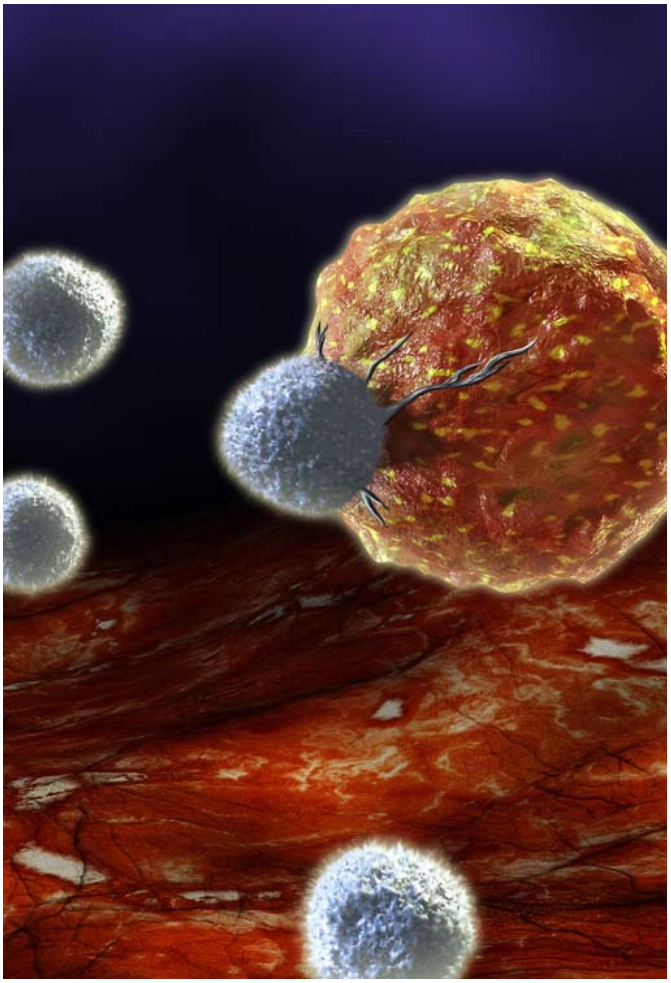
Cancer Treatment - Introduction

Cancer is uncontrolled growth and division of genetically altered cells that typically invade other tissues, may have the capacity to spread, and might eventually kill the patient.

Most cancer therapies attempt to stop this cell division by "poisoning" the cancer cells when they are dividing and most vulnerable. But cancer therapy also affects normal cells as they divide, often leading to unwanted side effects.

Cancer cells tend to divide continuously, which is why chemotherapy and radiotherapy are given over a number of days, weeks or months (in various forms and combinations) in the hope that the therapy will eventually kill all cancer cells.



Immune System Patterns - Emerging Evidence

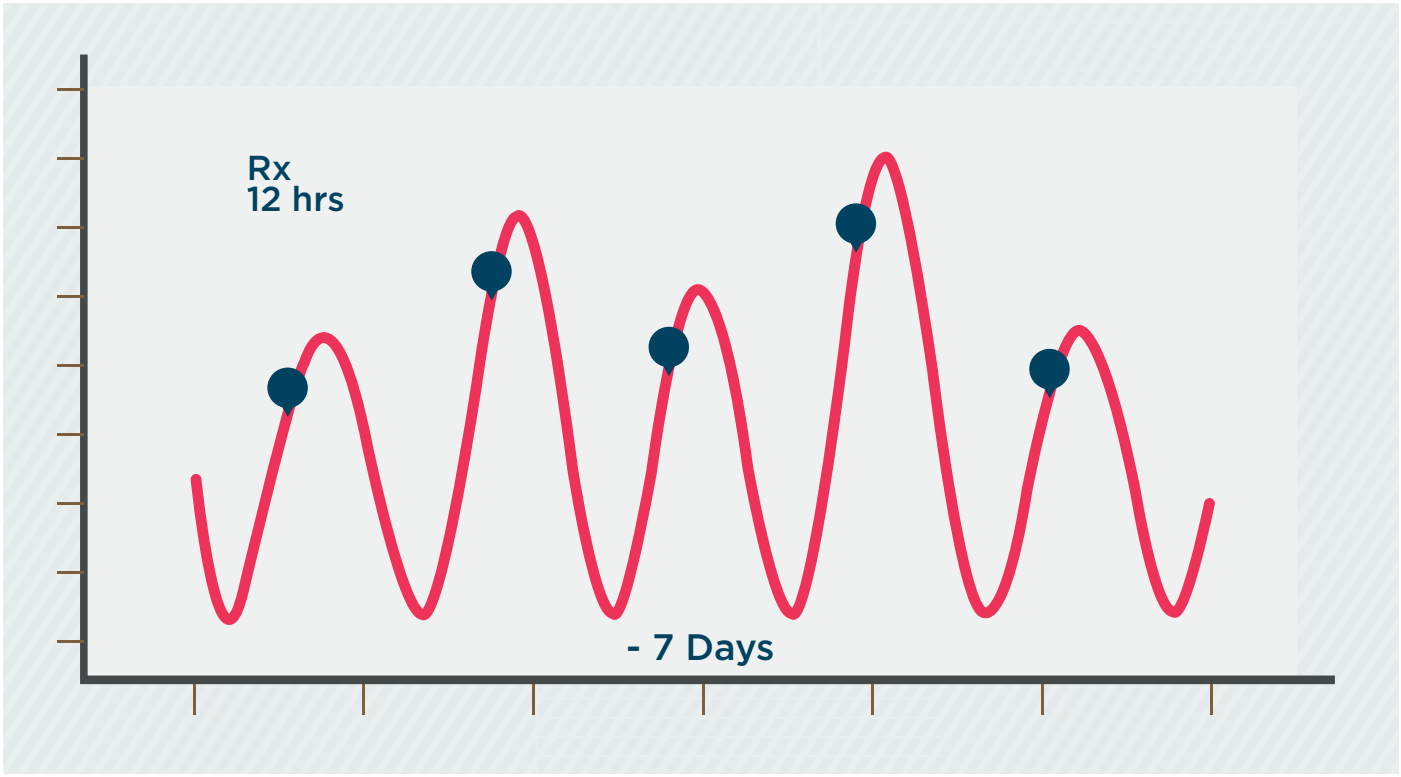
- For a long time it was thought the immune system is not aware of the cancer growing in the body. Evidence gathered over the past few years has made it clear that the immune system is not ignorant to the presence of the tumour. Like many things in nature which exist in a delicate balance, so too the immune system has finely tuned opposing forces of immunity and tolerance which repeats in a cyclical manner. This balance can allow vigorous immune responses towards infection and then stops to avoid damaging responses to normal healthy tissue.
- Once triggered, the immune system works in a very controlled, sequential and time-dependent fashion over several days, it switches "on" and "off" in sequence. Observations suggest that, in cancer, this "on/off" cycle simply repeats constantly under complex feedback control. In fact, this complex regulation is likely to be the very problem that prevents the immune system from gaining sufficient momentum to destroy the cancer.

The "on-switch" cells (T-Effector cells) "push" to kill the cancer by recruiting specialized white cells that can destroy cancer cells. The "off-switch" cells (T-Regulatory cells) act as opposing forces that slow down this response and control the T-Effector cells by keeping them at check. Both T-Effector and T-Regulatory cells divide synchronously over a very short time frame, a few days apart, unlike the cancer cells that divide slowly and continuosly. These immune cells can be selectively killed with standard cancer drugs by timing the administration to when they are dividing. If the therapy is timed correctly, the "off switch" cells can be removed, allowing the "un-regulated" immune system to kill the tumour cells. This has been shown in a number of mouse cancer models (see references).

Immune Cycle and the Timing of Treatment

In 2010, Biotempus researchers reported the discovery of a repeating “immune cycle”. Using serial blood measurements of C-reactive protein (CRP), a commonly used inflammatory marker, they mapped rises and falls over several days showing the initiation and termination of the immune response. These immune cycles most likely represent cyclical immune activation and suppression against the cancer, with a cycle period of approximately 5–8 days.

Researchers were further able to show that the timing of cancer therapy with respect to this cycle could be crucial in determining the success of treatment. By sequentially measuring CRP before and around the time of treatment, they were able to establish the position of the patient’s underlying immune curve (Fig. 1). They have been able to correlate the timing of chemotherapy with a 12-hour window with the induction of a more successful clinical response.



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In Summary

The cancer patient’s immune system oscillates or cycles.

It is proposed that this cycle creates narrow recurring therapeutic windows where the immune system can be manipulated to destroy the cancer.

We wish to test and document this in our canine cancer patients

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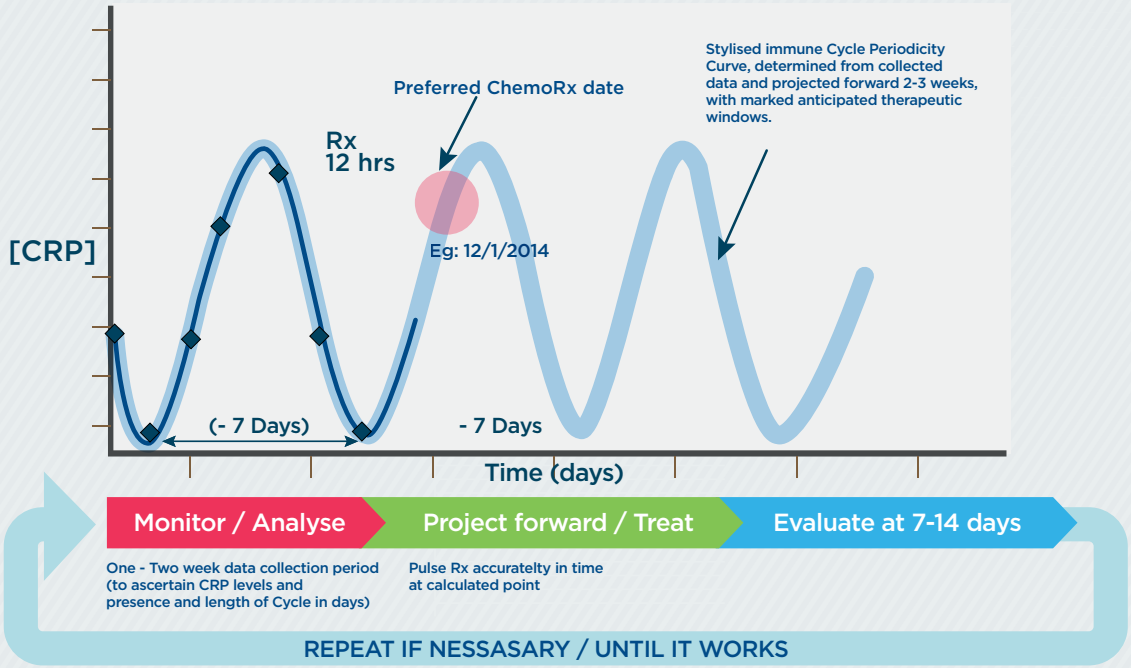
Dog Immune Monitoring & Treatment Schematics

Cytotoxic Chemotherapy Protocol



Process Steps – Canine Project Summary

An initial visit with your veterinarian will be scheduled to go over the details and sign an **Owner's Consent Form**

Serial Blood tests are performed (daily or every 2nd day) over 1-2 weeks at your veterinarian's clinic

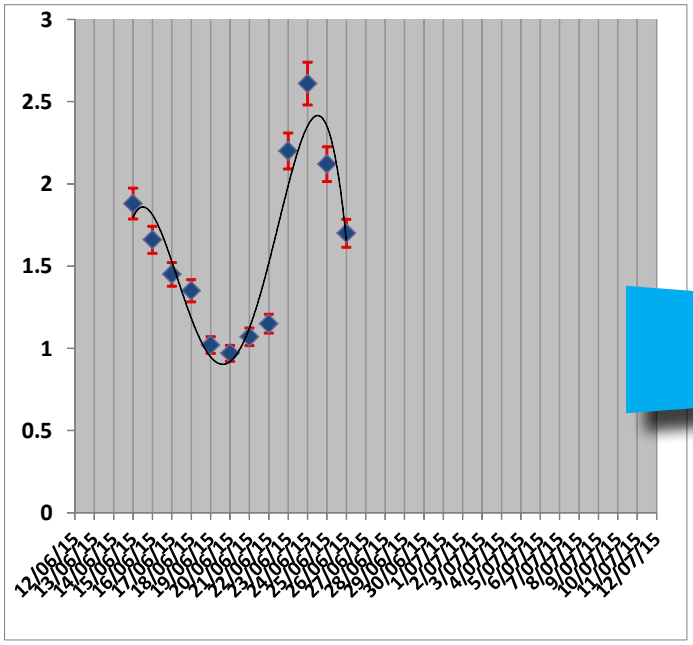
Data is applied to our algorithm and a report sent back to the veterinarian with optimal treatment time

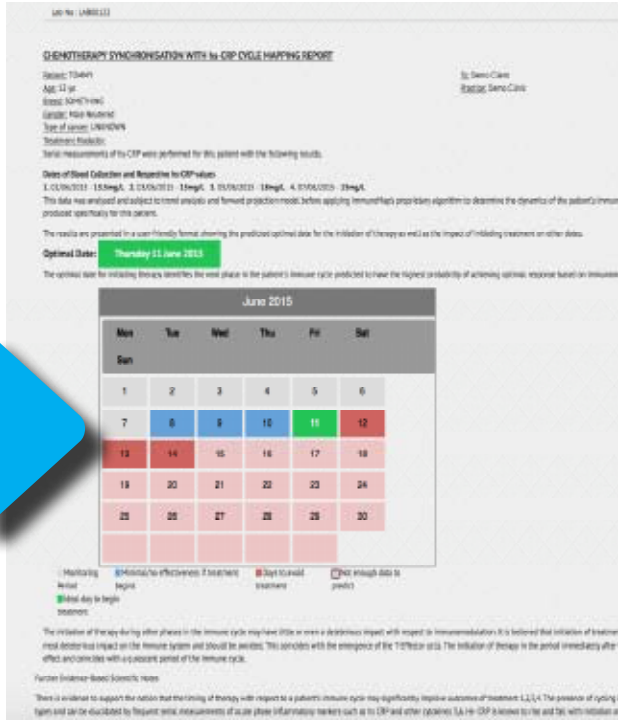
Treatment is provided by the veterinarian

Response is evaluated

These steps are repeated if necessary

Data is subject to trend analysis -> Report sent back to the veterinarian with optimal treatment time





Oral Cyclophosphamide tablets are prescribed by the veterinarian and administered by the veterinarian or pet owner

Repeat above for the next 1-2 cycles

About the treatment agent

Cyclophosphamide is a known chemotherapy agent.

In our trial Cyclophosphamide will be used as an immuno-therapeutic agent by using its ability to kill rapidly dividing cells. Administered at the suggested time window, it will be targeting T-Regulatory lymphocytes at the time they are dividing and vulnerable.

The expected result is tipping the balance of circulating T-Effector cell to / T-Regulatory cell populations in favor of the effector mechanism. It is postulated this will allow the immune system to overcome strong tumour regulation and eliminate the cancer.

Notes:

- Inclusion Criteria: Dogs must have measureable disease with elevated CRP. Please note that not all dogs with cancer will have CRP elevation. In most cases CRP is elevated in the serum of late stage cancer patients, rises with disease progression and returns to normal levels with successful treatment. We estimate that in 10% of patients a discrete immune cycle cannot be mapped in the first trial.
- No costs are associated with CRP measurements or treatment for this study. There will be veterinary clinic costs associating with managing the case by the treating veterinarian.
- Please review Owner Consent Form

OWNER CONSENT FORM

Study Summary

Our clinic is participating in a study investigating the association between cancer and the immune cycle in dogs.

Enabling your dog to participate in this study will hopefully shed further light on the role of the immune cycle plays in cancer and how we can use it to gain better outcomes in dogs. It may help the development of a better understanding of the importance of **timing** in the treatment of cancer in dogs in the future.

Owner Declaration

By participating in this study I am aware that several serum samples will be collected from my dog and that chemotherapy will be given to my dog for the purpose of research. I acknowledge that the procedures involved in this study are not different to those that would normally be performed in treating, diagnosing or monitoring cancer in dogs and that there are no additional risks involved to my dog.

Please Print

I, _____(your full name), owner of _____ (pet's name) provide consent and authorise the participation of my dog in this study.

Signature: _____

Date: _____

Attending Veterinarian Signature: _____

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